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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,301	12/17/2001	Lisa McKerracher	12552-003001/06447-002-US	1730

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,301	MCKERRACHER ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24, 28-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24 and 28-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Turner, Art Unit 1649.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-16-05 has been entered.

3. The amendment filed 3-18-05 has been entered into the record and has been fully considered. Claims 22-24, and 28-39 are pending.

4. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

5. As a result of applicant's amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 22-24, and 28-39 are rejected under 35 U.S.C. 112, first paragraph, as

failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 22-24, and 28-39 are newly presented. The claims enjoy support from the specification as outlined within the claims at pp. 9-12 of the amendment filed 8-20-04. However, the citations noted therein do not support the recitations and combinations of elements as newly recited as follows;

Claim 23 newly notes the compound structures as in (i) and (ii) with reference to paragraph 0021 and claim 1 of the '834 patent. While paragraph 21 refers to the '834 patent, the paragraph supports the recitation where "compounds such as Y-27632 (US 4,997,834), that block Rho-associated kinase activity, ... are embodiments of this invention and "the use of other compounds within this family of compounds that inhibit Rho kinase are also considered within the scope of this invention."

The specification now incorporates by reference a scope of the full noted structures of the '834 claim 1 and imports recitations directed to Rho-family member-mediated inhibition of neuronal axon growth and a Rho family antagonist that antagonizes Rho-associated kinase activity. While the specification notes such activities with Y-27632, no other compounds or scope of compounds appear to be noted as providing for the noted functional recitations. Moreover, the specification does not apparently support the combination for the selection of antagonists to be used via the noted functional activities of stimulating regenerative growth of damaged neuronal

axons past the lesion site and wherein the antagonist has the ability, when triturated into primary retinal ganglion cells in vitro to produce outgrowth of retinal ganglion cell neurites, the retinal ganglion cells being plated on a growth inhibitory substrate selected from the group consisting of myelin and chondroitin sulfate proteoglycan' as now claimed. There is no evidence that any other compounds possess such functional activities.

Applicants argue in the 3-18-05 response that the amendments to the claims obviate rejection with respect to a proper incorporation by reference as delineated within the response via reference to the 4,997,834 patent, the specification at pp. 5 and 9-10 and noted via reference Uehata, 1997.

Applicants arguments filed 3-18-05 have been fully considered and are persuasive in part, to the extent of Y27632, but does not extend to compounds that are pharmaceutically acceptable addition salts thereof or to compounds within the formula of claim 23, other than Y27632. The evidence does not correlate with the full scope of the claims sufficient to show that the structural and functional constraints recited are correlated to suppression of Rho family member-mediated inhibition and antagonism of rho-associated kinase activity.

The Examiner acknowledges Applicants referral to the specification at pp. 5 and 9-10. For clarification, the art recognizes the recited compounds as recognized in the art, see in particular US Patent 4,997,834 (note correction of the patent number from previous notation). A review of the prior art also evidences knowledge by the artisan of "Rho-associated kinase" p164 as in Matsui et al., EMBO J., 15(9):2208-16, 1996. The

artisan further recognizes such activity and assays for such activity, see further IDS references, Amano et al., J. Biol. Chem. 1996 Aug23, 271(34):20246-9, Kimura et al., Science 1996 July 12, 273(5272):245-8 in addition to Applicants reference to Uehata et al., 1997, Nature 389:990-994. Thus, the art evidences a single species member Y-27632 which provides for the noted function of antagonizing Rho-associated kinase activity and is evidenced to suppress Rho family member mediated inhibiton of neuronal axon growth.

However, the claims encompass a large genus of compounds comprising "pharmaceutically acceptable addition salts thereof" and a multitude of compounds falling within the scope of the recited generic formula, none of which are evidenced to exhibit the functional activities of either antagonizing Rho-associated kinase activity or for suppression of Rho family member-mediated inhibition of neuronal axon growth other than the single compound of Y27632. The single species member does not adequately support the genus or evidence that applicants were in possession of the full genus. There is no supportive evidence of a correlation between the noted structurally related compounds and the recited biological functions. Nor is there any evidence that any other member, other than Y27632, with the recited structure would be sufficient to provide for the instantly claimed activities. Such structure function relationships amongst biological molecules and various pharmaceutical compounds are inherently unpredictable and require experimental testing related to the structure compounds and its biological target. For example Caporale et al., PNAS 92:75-82, 1995 notes that "it is still beyond our capability to design, routinely, such lead structures, based simply upon

knowledge of the structure of our target." As the art fails to evidence any conserved structure amongst the noted molecules capable of reproducing similar activity in mediating neuronal outgrowth or inhibition of Rho-associated kinase activity, and the compounds noted were not specifically designed for such action, the artisan cannot conclude that the single member adequately describes a genus of molecules capable of such functions. Thus, the specification lacks adequate written description support for the invention claimed. Evidence that any other structural member falling within the scope of the claim actually provides for the noted activities would further prosecution.

8. Claims 22-24, and 28-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for y27632, does not reasonably provide enablement for the full scope of the other compounds encompassed as directed to pharmaceutically acceptable addition salts thereof and compounds within the structural formula of claim 23 that exhibit the ability to suppress Rho family member–mediated inhibition of neuronal axon growth and antagonizes Rho-associated kinase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working

examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Claim 23 newly notes the compound structures as in (i) and (ii) with reference to paragraph 0021 and claim 1 of the '834 patent. While paragraph 21 refers to the '834 patent, the paragraph supports the recitation where "compounds such as Y-27632 (US 4,997,834), that block Rho-associated kinase activity, ... are embodiments of this invention and "the use of other compounds within this family of compounds that inhibit Rho kinase are also considered within the scope of this invention."

The specification now incorporates by reference a scope of the full noted structures of the '834 claim 1, and imports recitations directed to Rho-family member-mediated inhibition of neuronal axon growth and a Rho family antagonist that antagonizes Rho-associated kinase activity. While the specification notes such activities with Y-27632, no other compounds or scope of compounds appear to be noted as providing for the noted functional recitations. Moreover, the specification does not apparently support the combination for the selection of antagonists to be used via the noted functional activities of stimulating regenerative growth of damaged neuronal axons past the lesion site and wherein the antagonist has the ability, when triturated into primary retinal ganglion cells in vitro to produce outgrowth of retinal ganglion cell neurites, the retinal ganglion cells being plated on a growth inhibitory substrate selected from the group consisting of myelin and chondroitin sulfate proteoglycan' as now claimed. There is no evidence that any other compounds possess such functional activities.

Such enablement with respect to Y27632 does not extend to compounds that are pharmaceutically acceptable addition salts thereof or to compounds within the formula of claim 23, other than Y27632. The evidence does not correlate with the full scope of the claims sufficient to show that the structural and functional constraints recited are correlated to suppression of Rho family member-mediated inhibition and antagonism of rho-associated kinase activity or of "rho-kinase".

The Examiner acknowledges Applicants referral to the specification at pp. 5 and 9-10. For clarification, the art recognizes the recited compounds as recognized in the art, see in particular US Patent 4,997,834 (note correction of the patent number from previous notation). A review of the prior art also evidences knowledge by the artisan of "Rho-associated kinase" p164 as in Matsui et al., EMBO J., 15(9):2208-16, 1996. The artisan further recognizes such activity and assays for such activity, see further IDS references, Amano et al., J. Biol. Chem. 1996 Aug23, 271(34):20246-9, Kimura et al., Science 1996 July 12, 273(5272):245-8 in addition to Applicants reference to Uehata et al., 1997, Nature 389:990-994. Thus, the art evidences a single species member Y-27632 which provides for the noted function of antagonizing Rho-associated kinase activity and is evidenced to suppress Rho family member mediated inhibiton of neuronal axon growth.

However, the claims encompass a large genus of compounds comprising "pharmaceutically acceptable addition salts thereof" and a multitude of compounds falling within the scope of the recited generic formula, none of which are evidenced to exhibit the functional activities of either antagonizing Rho-associated kinase activity or

for suppression of Rho family member-mediated inhibition of neuronal axon growth other than the single compound of Y27632. The single species member does not adequately support the genus or evidence that applicants were in possession of the full genus. There is no supportive evidence of a correlation between the noted structurally related compounds and the recited biological functions. Nor is there any evidence that any other member, other than Y27632, with the recited structure would be sufficient to provide for the instantly claimed activities. Such structure function relationships amongst biological molecules and various pharmaceutical compounds are inherently unpredictable and require experimental testing related to the structure compounds and its biological target. For example Caporale et al., PNAS 92:75-82, 1995 notes that "it is still beyond our capability to design, routinely, such lead structures, based simply upon knowledge of the structure of our target." As the art fails to evidence any conserved structure amongst the noted molecules capable of reproducing similar activity in mediating neuronal outgrowth or inhibition of Rho-associated kinase activity, and the compounds noted were not specifically designed for such action, the artisan cannot conclude that the single member adequately describes a genus of molecules capable of such functions. Thus, the specification lacks adequate written description support for the invention claimed. Evidence that any other structural member falling within the scope of the claim actually provides for the noted activities would further prosecution.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the

experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation.

Accordingly, the skilled artisan cannot readily make and use the recitations of the claims without further undue experimentation. The recited structural and functional combinations are not evidenced or exemplified and determination of such is beyond routine experimentation in the art.

Status of Claims

9. No claims are allowed.

Conclusion

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Thursday from

7:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at (571) 272-0867.

Sharon L. Turner, Ph.D.
July 24, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER

7-24-05